REMARKS

Claims 34-36, 41-42, 53-56 and 59-64 are all the claims pending in the application. Claims 1-33, 37-40, 43-52 and 57-58 have been canceled. Claims 34-35, 42, 60-61 and 64 have been amended. Support for the claim amendments can be found throughout the specification and originally filed claims.

Specifically, claim 34 originally depends from cancelled claim 35 and has been amended to be in an independent form. Moreover, claims 35-36, 41-42 and 55 also originally depend from cancelled claim 35 and have been amended to depend from claim 34 instead.

Claim 34 is further amended to recite "to encode a fusion protein between the PPIase and the desired protein" and "comprising an IF domain" as agreed with the Examiner during a telephone interview of March 25, 2009.

Claim 35 has been amended to recite "in which a third coding region is inserted, wherein the third coding region" as suggested by the Examiner in response to a §112, second paragraph rejection.

Claims 42 has been amended to clarify the claim language.

Claims 60 and 61 have been amended to recite "the" in place of "a" preceding each of cytoplasm, periplasm and medium as suggested by the Examiner in response to claim objections.

Claim 64 has been amended to recite "[a] process for producing a desired protein, which comprises producing a fused protein by the process of claim 59 and digesting the fused protein with a protease that digests the protease digestion site" as suggested by the Examiner in response to a §112, second paragraph rejection.

Accordingly, no new matter has been introduced by these amendments to claims.

I. Claim Objections

Claims 60 and 61 are objected to because of the following informalities: the recitation of "to produce the fused protein in a cytoplasm of said host cell" in claim 60 and "to produce the fused protein in a periplasm or a medium of said host cell" in claim 61 imply that a host cell includes more than one cytoplasm, periplasm or medium but this is not the case.

In response, Applicants have amended claims 60 and 61 to recite "the" in place of "a" preceding each of cytoplasm, periplasm and medium as suggested by the Office Action.

Accordingly, withdrawal of the above claim objections is respectfully requested.

II. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 35 and 64 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite.

1. The Examiner states that claim 35 is confusing as to whether the claim requires a sequence encoding a protease digestion site to actually be present in the claimed vector or if the vector only requires that a protease digestion site can be inserted therein.

In response, Applicants have amended claim 35 to replace "in which a second coding region can be inserted, wherein the region" with "in which a third coding region is inserted, wherein the third coding region" as suggested by the Office Action.

2. The Examiner states that the structure of claim 64 is such that it makes it unclear if the process of claim 59 is an active step of the process of claim 64 or not.

In response, Applicants have amended claim 64 to recite "[a] process for producing a desired protein, which comprises producing a fused protein by the process of claim 59 and

digesting the fused protein with a protease that digests the protease digestion site" as suggested by the Office Action.

Accordingly, withdrawal of the above rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

III. Claim Rejections Under 35 U.S.C. § 102

1. Claims 33, 35, 36, 42, 55, 56, 59, 60 and 64 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Iida *et al.* (GENE, Vol. 256, 2000; "Iida").

As pointed out in MPEP § 2131, "[t]o anticipate a claim, the reference must teach every element of the claim." Thus, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. Of California*, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987)." Applicants respectfully submit that the Iida reference fails to teach each and every element as set forth in the present claims.

Applicants have canceled claim 33 and amended claim 34 to be in an independent form, solely to expedite the prosecution. Applicants assert that the current amendments render moot all outstanding claim rejections at least because the cited art fails to disclose an expression vector "wherein the first coding region is operatively linked to a promoter" as recited in claim 34.

Specifically, in Iida's pGEX-HcFK-1, the DNA fragment encoding the FKSP-type PPIase is ligated into downstream of the site encoding GST and is not "operatively linked to a promoter" as recited in claim 34. On the other hand, in the presently claimed expression vector, a region into which a second coding region encoding a desired protein can be inserted is in the

downstream of the first coding region encoding a PPIase, and the first coding region is operatively linked to a promoter.

Claims 35, 36, 42, 55, 56, 59, 60 and 64 depend directly or indirectly from independent claim 34.

Accordingly, as Iida fails to disclose an expression vector "wherein the first coding region is operatively linked to a promoter" as recited in independent claim 34, Applicants respectfully request that this anticipation rejection under 35 U.S.C. § 102 be reconsidered and withdrawn.

2. Claims 33, 41, 42, 55 and 56 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Furutani *et al.* (Biochemistry, 2000, 39(2); "Furutani").

As pointed out in MPEP § 2131, "[t]o anticipate a claim, the reference must teach every element of the claim." Thus, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. Of California*, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987)." Applicants respectfully submit that the Furutani reference fails to teach each and every element as set forth in the present claims.

Applicants have canceled claim 33 and amended claim 34 to be in an independent form, solely to expedite the prosecution. Applicants assert that the current amendments render moot all outstanding claim rejections, at least because the cited art fails to disclose "a region having at least one restriction enzyme site in the same reading frame as the first coding region [encoding a PPIase] into which a second coding region encoding a desired protein can be

inserted to encode a fusion protein between the PPIase and the desired protein ... wherein ... the restriction enzyme site is downstream of the first coding region." as recited in claim 34.

Specifically, in making the rejection, the Examiner asserts that Furutani teaches an expression vector having a BamHI restriction site following the FKBP-type PPIase coding sequence. However, Applicants respectfully point out that Furutani's expression vector, pTFK, has a termination codon between the PPIase site and the BamHI restriction site. Page 454, lines 15-31 of Materials and Methods. Moreover, for Examiner's reference, Applicants submit hereinwith a diagram to summarize the making of Furutani's expression vector pTFK. Thus, as the diagram based on the disclosure of Furutani shows, the BamHI restriction site is not "in the same reading frame as the first coding region [encoding a PPIase]" in Furutani's expression vector as recited in claim 34.

Moreover, the other restriction enzyme site, NcoI, is located upstream of the FKBP-type PPIase coding sequence and is not "downstream of the first coding region [encoding a PPIase]" as recited in claim 34.

Additionally, Furutani is silent regarding any "a second coding region encoding a desired protein [that] can be inserted to encode a fusion protein between the PPIase and the desired protein" as recited in claim 34. In fact, because of the termination codon at the end of the FKBP-type PPIase coding sequence, Furutani's pTFK vector is incapable of producing any fusion protein.

Claims 41, 42, 55 and 56 depend directly or indirectly from independent claim 34.

Therefore, as Furutani fails to disclose "a region having at least one restriction enzyme site in the same reading frame as the first coding region into which a second coding region encoding a desired protein can be inserted to encode a fusion protein between the PPIase and the

desired protein ... wherein ... the restriction enzyme site is downstream of the first coding region" as recited in independent claim 34, Applicants respectfully request that this anticipation rejection under 35 U.S.C. § 102 be reconsidered and withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 103

1. Claims 34, 53, 54, 61, 62, and 63 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Scholz *et al.* (U.S. Patent Publication No. 2003/0096352; "Scholz") in view of Iida *et al.* (GENE, Vol. 256, 2000; "Iida").

In making the rejection, the Examiner admits that Scholz does not teach any "archaebacterial FKBP-type PPIase" as recited in claim 34. However, the Examiner states, "it would have been obvious to one of ordinary skill in the art to select the [archaebacterial FKBP-type] PPIase of *Halobacterium cutirubrum* [from Iida] for use in the fusion vectors of Scholz ..."

Applicants respectfully traverse for the following reasons.

First, Applicants submit that there is no reason why one of ordinary skill in the art would modify Scholz's expression vector to incorporate Iida's archaebacterial FKBP-type PPIase.

As the Supreme Court recently stated, the "apparent reason to combine the known elements in a fashion claimed by the [claims] at issue ... should be made explicit." *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 slip op. at 14 (U.S. Apr. 30, 2007). Rather than indicating why one of skill in the art would choose to combine the cited references in making an expression vector, the Examiner is silent.

Second, the presence of a property not possessed by the prior art is evidence of nonobviousness. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Applicants respectfully submit that the present invention teaches an unexpectedly superior property of the

claimed expression vector not possessed by Scholz's expression vector with a non-archaebacterial FKBP-type PPIase sequence or Iida's expression vector with glutathione S-transferase (GST) encoding region located upstream of a PPIase sequence.

Specifically, the presently claimed expression vector possesses an unexpectedly superior property in that it to produces a fused protein with hardly expressible proteins in a soluble form in a large amount and effectively. Summary of Invention, page 4, lines 14-21, page 13, line 11-page 14, line 14, page 28, line 32-page 29, line 3, and Examples 1-3.

On the other hand, Scholz's expression vector with a non-archaebacterial FKBP-type PPIase sequence without an IF domain does not possess such an unexpectedly superior property of the claimed expression vector with an archaebacterial FKBP-type PPIase sequence comprising an IF domain. In Scholz, a recombinant fusion protein comprising one polypeptide sequence corresponding to a FKBP chaperone selected from the group consisting of FkpA, SlyD and trigger factor and one polypeptide sequence corresponding to a target peptide is produced. [0060] Although Scholz states that the fusion protein has "advantageous properties, e.g., with regard to solubilization," Scholz's fusion protein is initially obtained in form of "inclusion bodies" and then is solubilized by chaotropic solubilization. [0015], [0060]-[0069] and Examples.

The present invention provides an expression vector producing a fusion protein as a natural type, that is, "a soluble type," Thus, the fusion protein is produced in "a soluble type," not in "inclusion bodies." For this purpose, as an important technical feature, the expression vector of the invention have a first coding region encoding archaebacterial FKBP-type PPIase.

As the Examiner admits at page 3 of the Office Action, Applicants previously have provided sufficient information to conclude that the IF domain of archaebacterial FKBP-type PPIase is critical for chaperone function of the PPIases and that other proteins with chaperone

function but lacking any IF domain, such as Scholz's non-archaebacterial FKBP-type PPIase, do not show the same results. *See* Page 3, Examiner's Office Action of April 3, 2009; Applicants' Amendments filed February 20, 2009 and May 19, 2008; 1.132 Declaration of Dr. Ideno filed on November 9, 2007; Furutani et al., Biochemistry, 39 (2), 453-462, 2000; Suzuki et al., J. Mol. Biol, 328, 1149-1160, 2003; Maruyama et al., Frontiers in Bioscience, 5, 821-836, 2000; Ideno, et al., WO 2005/063964, filed on December 24, 2004.

Moreover, Iida's expression vector with a GST encoding region located upstream of a PPIase does not possess such an unexpectedly superior property of the claimed expression vector with a desired protein encoding region located downstream of an archaebacterial FKBP-type PPIase. When the desired protein is expressed before the PPIase, the protein forms an inactive abnormal structure instantly without the PPIase to prevent such formation, and the resulting fused protein with a hardly expressible protein would not be in the active soluble form.

For the foregoing reasons, Applicants respectfully submit that the claims are not rendered obvious by the cited references and request that this rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

2. Claims 34-36, 53, 54, and 60-64 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Scholz *et al.* (U.S. Patent Publication No. 2003/0096352; "Scholz") in view of Furutani *et al.* (Biochemistry, 2000, 39(2); "Furutani").

In making the rejection, the Examiner admits that Scholz does not teach any "archaebacterial FKBP-type PPIase" as recited in claim 34. However, the Examiner states, "it would have been obvious to one of ordinary skill in the art to select the [archaebacterial FKBP-

type] PPIase of *Methanococcus thermolithotrophicus* [from Furutani] for use in the fusion vectors of Scholz ..."

Applicants respectfully traverse for the following reasons.

First, Applicants submit that there is no reason why one of ordinary skill in the art would modify Scholz's expression vector to incorporate Furutani's archaebacterial FKBP-type PPIase.

As the Supreme Court recently stated, the "apparent reason to combine the known elements in a fashion claimed by the [claims] at issue ... should be made explicit." *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 slip op. at 14 (U.S. Apr. 30, 2007). Rather than indicating why one of skill in the art would choose to combine the cited references in making an expression vector, the Examiner is silent.

Moreover, as pointed out in MPEP § 2143.01, "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)." Scholz's expression vector is intended to express a fusion protein. However, as discussed above, Furutani's PPIase encoding sequence contains a termination codon at the end, which prevents producing a fusion protein. Thus, if Scholz's expression vector is modified to incorporate Furutani's PPIase encoding sequence in place of Scholz's PPIase encoding sequence, the resulted expression vector will be incapable of producing any fusion protein. Accordingly, there is no suggestion or motivation for one of ordinary skill in the art to modify Scholz's expression vector to incorporate Furutani's archaebacterial FKBP-type PPIase.

Second, the presence of a property not possessed by the prior art is evidence of nonobviousness. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). As discussed above, the presently claimed expression vector possesses an unexpectedly superior property in that it

produces a fused protein with hardly expressible proteins in a soluble form in a large amount and effectively. Summary of Invention, page 4, lines 14-21, page 13, line 11-page 14, line 14, page 28, line 32-page 29, line 3, and Examples 1-3.

On the other hand, such an unexpectedly superior property of the claimed expression vector is not possessed by Scholz's expression vector with a non-archaebacterial FKBP-type PPIase sequence, as discussed above, or Furutani's expression vector, which is even incapable of producing a fusion protein.

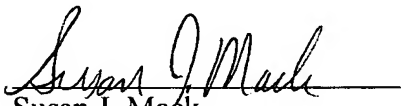
For the foregoing reasons, Applicants respectfully submit that the claims are not rendered obvious by the cited references and request that this rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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